

RESEARCH  
UPDATES

FOR THE LATEST IN WORLDWIDE INTEGRATED CANCER CARE

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**IN THIS ISSUE:** Do you remember your grandma's nagging words, "An apple a day keeps the doctor away"? Trust her wisdom; Jedrychowski and colleagues report that the consumption of one apple a day reduced the risk of developing colorectal cancer by 35%. Eating more than one apple per day reduced the risk by 50%.

This issue highlights a collection of studies that stress the importance of nutrition for cancer prevention. For instance, high consumption of citrus fruit had a protective effect against cancer of the digestive and upper respiratory tract; women who stuck to a diet that was geared toward optimal health and cancer prevention may reap benefits even after a diagnosis of ovarian cancer; whereas the consumption of eggs and poultry may increase the risk of prostate cancer recurrence or progression. There are also two fascinating reports regarding green tea consumption.

In addition, Block and colleagues describe the benefits of an integrated approach that respects and supports the natural circadian rhythm for colon cancer patients. Also, Lengacher et al. report that mindfulness-based stress reduction significantly improves the psychological status and quality of life in breast cancer survivors.

In our study of the month, Pace et al. report on strong clinical evidence that vitamin E can reduce the risk of neurotoxicity from chemotherapy.



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## NUTRITION

Jedrychowski, W, U. Maugeri, T. Popiela, et al.

### Case-Control Study on Beneficial Effect of Regular Consumption of Apples on Colorectal Cancer Risk in a Population with Relatively Low Intake of Fruits and Vegetables.

*European Journal of Cancer Prevention.* 2010 Jan; 191:42-47.

Laboratory in-vitro studies and animal experiments showing the potential health benefits from apples raises the question to what extent the regular consumption of apples in humans may have a beneficial effect on colorectal cancer risk. A total of 592 incident cases of colorectal cancer have been enrolled in a hospital-based case-control study. The comparison group included 765 controls chosen from the patients of the same hospital without history of cancer and admitted for treatment of nonneoplastic conditions. Interviews of both cases and controls were conducted in the hospital setting by trained interviewers. The median intake of fruits among cases was lower than in controls (9.5 vs. 11 servings/week) and the difference was statistically significant.

Apples were the most frequent fruit consumed by the study participants and about 80% of variability in the total fruit consumption resulted from the intake of apples. We did not observe any significant statistical differences in consumption of berries, citrus, or stone fruits and other kinds of fruits across cases and controls. The adjusted estimates of colorectal cancer risk related to the daily consumption of apples (in quintiles) were based on the unconditional multivariate logistic model, which considered the set of potential confounding variables such as demographic characteristics of participants (age, gender, place of residency, marital status, tobacco smoking), total energy intake, intake of vegetables and fruits without apples. The results of the logistic analysis showed that the adjusted risk of colorectal cancer inversely correlated with daily number of apple servings.



**BOTTOM LINE:** The reduced risk of colorectal cancer of border significance level was already observed at the consumption of at least one apple a day (odds ratio=0.65, 95% CI: 0.39-1.09), **but at the intake of more than one apple a day the risk was reduced by about 50%** (odds ratio=0.53, 95% CI: 0.35-0.79). Neither the consumption of vegetables nor other fruits have shown beneficial effects on the risk of colorectal cancer. The observed protective effect of apple consumption on colorectal risk may result from their rich content of flavonoid and other polyphenols, which can inhibit cancer onset and cell proliferation. **INSPIREHEALTH'S INTERPRETATION:** An apple a day keeps the doctor away!

Foschi, R, Claudio Pelucchi, Luigino Dal Maso, et al.

### Citrus Fruit and Cancer Risk in a Network of case-control Studies

*Cancer Causes & Control.* 2010 02; 212: 237-242.

**BACKGROUND:** Citrus fruit has shown a favorable effect against various cancers. To better understand their role in cancer risk, we analyzed data from a series of case-control studies conducted in Italy and Switzerland. **PATIENTS AND METHODS:** The studies included 955 patients with oral and pharyngeal cancer, 395 with esophageal, 999 with stomach, 3,634 with large bowel, 527 with laryngeal, 2,900 with breast, 454 with endometrial, 1,031 with ovarian, 1,294 with prostate, and 767 with renal cell cancer. All cancers were incident and histologically confirmed. Controls were admitted to the same network of hospitals for acute, nonneoplastic conditions. Odds ratios (OR) were estimated by multiple logistic regression models, including terms for major identified confounding factors for each cancer site, and energy intake.

**RESULTS:** The ORs for the highest versus lowest category of citrus fruit consumption were 0.47 (95% confidence interval, CI, 0.36-0.61) for oral and pharyngeal, 0.42 (95% CI, 0.25-0.70) for esophageal, 0.69 (95% CI, 0.52-0.92) for stomach, 0.82 (95% CI, 0.72-0.93) for colorectal, and 0.55 (95% CI, 0.37-0.83) for laryngeal cancer. No consistent association was found with breast, endometrial, ovarian, prostate, and renal cell cancer.

**CONCLUSIONS:** Our findings indicate that citrus fruit has a protective role against cancers of the digestive and upper respiratory tract.

Dolecek, TA, B. J. McCarthy, C. E. Joslin, et al.

### Prediagnosis Food Patterns are Associated with Length of Survival from Epithelial Ovarian Cancer.

*J Am Diet Assoc.* 2010 March; 1103: 369-382.

**BACKGROUND:** Dietary factors have been the focus of many studies on the etiology of ovarian cancer and may potentially affect survival. Indeed, three recent studies outside the United States have suggested that diet plays a role in ovarian cancer survival. **OBJECTIVE:** The study purpose was to evaluate the hypothesis that women diagnosed with ovarian cancer whose reported prediagnosis food patterns more closely reflect recommendations for optimal health experience a survival advantage compared with those reporting poorer diets. **DESIGN:** A longitudinal follow-up study design was used to examine prediagnosis usual diet effects on survival among 341 Cook County, Illinois, residents diagnosed with epithelial ovarian cancer during 1994-1998. These women participated in a previous case-control study where diet was assessed using a validated food frequency questionnaire. This diet information was categorized utilizing the Dietary Guidelines for Americans 2005. Deaths through 2005 were ascertained using a national death index search. **STATISTICAL ANALYSIS:** Hazard ratios (HR) and 95% confidence intervals (CI) adjusting for important covariables were obtained from proportional hazards regression models to evaluate diet effects on survival from ovarian cancer.

**RESULTS:** Comparisons of high to low food group or subgroup intakes demonstrated statistically significant prediagnosis food pattern associations with survival time. Longer survival was associated with total fruits and vegetables (HR 0.61, 95% CI 0.38 to 0.98, P for trend=0.10) and vegetables separately (HR



0.66, 95% CI 0.43 to 1.01, P for trend <0.05). Subgroup analyses showed only yellow and cruciferous vegetables to significantly favor survival. Conversely, a survival disadvantage was shown for meats, not generally recommended (HR 2.28, 95% CI 1.34 to 3.89, P for trend <0.01), and specifically the red and cured/processed meats subgroups. An increased HR was also observed for the milk (all types) subgroup (HR 2.15, 95% CI 1.20 to 3.84, P for trend <0.05).

**CONCLUSIONS:** Prediagnosis adherence to diets that reflect recommendations for optimal nutrition and cancer prevention may have benefits that continue even after an ovarian cancer diagnosis.

Richman, EL, M. J. Stampfer, A. Paciorek, J. M. et al.

**Intakes of Meat, Fish, Poultry, and Eggs and Risk of Prostate Cancer Progression.**  
*Am J Clin Nutr.* 2010 01 Mar; 913: 712-721.

**BACKGROUND:** Processed meat and fish have been shown to be associated with the risk of advanced prostate cancer, but few studies have examined diet after prostate cancer diagnosis and risk of its progression. **OBJECTIVE:** We examined the association between postdiagnostic consumption of processed and unprocessed red meat, fish, poultry, and eggs and the risk of prostate cancer recurrence or progression.

**DESIGN:** We conducted a prospective study in 1294 men with prostate cancer, without recurrence or progression as of 2004-2005, who were participating in the Cancer of the Prostate Strategic Urologic Research Endeavor and who were followed for an average of 2 y.

**RESULTS:** We observed 127 events (prostate cancer death or metastases, elevated prostate-specific antigen concentration, or secondary treatment) during 2610 person-years. Intakes of processed and unprocessed red meat, fish, total poultry, and skinless poultry were not associated with prostate cancer recurrence or progression. Greater consumption of eggs and poultry with skin was associated with 2-fold increases in risk in a comparison of extreme quantiles: eggs [hazard ratio (HR): 2.02; 95% CI: 1.10, 3.72; P for trend = 0.05] and poultry with skin (HR: 2.26; 95% CI: 1.36, 3.76; P for trend = 0.003). An interaction was observed between prognostic risk at diagnosis and poultry. Men with high prognostic risk and a high poultry intake had a 4-fold increased risk of recurrence or progression compared with men with low/intermediate prognostic risk and a low poultry intake (P for interaction = 0.003).

**CONCLUSIONS:** Our results suggest that the postdiagnostic consumption of processed or unprocessed red meat, fish, or skinless poultry is not associated with prostate cancer recurrence or progression, whereas consumption of eggs and poultry with skin may increase the risk.

Ogunleye, AA, F. Xue and K. B. Michels.

**Green Tea Consumption and Breast Cancer Risk Or Recurrence: A Meta-Analysis.**

*Breast Cancer Research & Treatment.* 2010 Jan; 1192: 477-484.

Green tea is a commonly consumed beverage in Asia and has been suggested to have anti-inflammatory and possible anti-carcinogenic properties in laboratory studies. We sought to examine the association between green tea consumption and risk of breast cancer incidence or recurrence, using all available epidemiologic evidence to date. We conducted a systematic search of five databases and performed a meta-analysis of studies of breast cancer risk and recurrence published between 1998 and 2009, encompassing 5,617 cases of breast cancer. Summary relative risks (RR) were calculated using a fixed effects model, and tests of heterogeneity across combined studies were conducted. We identified two studies of breast cancer recurrence and seven studies of breast cancer incidence.

**RESULTS:** Increased green tea consumption (more than three cups a day) was inversely associated with breast cancer recurrence (Pooled RR = 0.73, 95% CI: 0.56-0.96). An analysis of case-control studies of breast cancer incidence suggested an inverse association with a pooled RR of 0.81 (95% CI: 0.75, 0.88) while no

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association was found among cohort studies of breast cancer incidence. Combining all studies of breast cancer incidence resulted in significant heterogeneity.

**CONCLUSIONS:** Available epidemiologic evidence supports the hypothesis that increased green tea consumption may be inversely associated with risk of breast cancer recurrence. The association between green tea consumption and breast cancer incidence remains unclear based on the current evidence. **INSPIREHEALTH'S INTERPRETATION:** Drinking more than 3 cups of green tea has a 27% protective effect on breast cancer recurrence.

Deandrea, S, R. Foschi, C. Galeone, et al.

### Is Temperature an Effect Modifier of the Association between Green Tea Intake and Gastric Cancer Risk?

*European Journal of Cancer Prevention.* 2010 Jan; 191: 18-22.

We considered the relationship between green tea and gastric cancer risk in Harbin, Heilongjiang province, Northeast China, an area with high baseline risk of stomach cancer. We used data from a case-control study conducted from 1987 to 1989 among 266 incident cases of stomach cancer and 533 controls admitted to the same hospitals as cases, with non-neoplastic and non-gastric diseases. **RESULTS:** No association emerged when tea consumption alone was considered: the odds ratio (OR) for green tea consumption was 0.87 (95% CI: 0.60-1.25) for green tea intake  $\geq$  750 g/year versus no intake and 0.99 (95% CI: 0.97-1.02) for an increment of 500 g of tea per year. When tea consumption was classified according to the temperature, however, the **OR was 0.19** (95% CI: 0.07-0.49) for lukewarm tea intake  $\geq$  750 g/year and 1.27 (95% CI: 0.85-1.90) for hot tea intake (P value for interaction  $<0.001$ ) as compared with non-drinkers. The corresponding ORs for an increment of 500 g of tea per year were 0.61 (95% CI: 0.45-0.82) and 1.03 (95% CI: 0.99-1.07) for lukewarm and hot tea, respectively (P value for interaction  $<0.001$ ).

**CONCLUSIONS:** We found an inverse relationship between green tea drinking and gastric cancer risk limited to the intake of lukewarm tea. **INSPIREHEALTH'S INTERPRETATION:** Consumption of lukewarm green tea, rather than hot tea, had an 81% protective effect on the development of gastric cancer.

## INTEGRATIVE CANCER CARE

Block, KI, P. B. Block, S. R. Fox, et al.

### Making Circadian Cancer Therapy Practical.

*Integrative Cancer Therapies.* 2009 Dec; 84: 371-386.

Practical circadian therapy for the cancer patient involves 3 spheres of intervention—improving lifestyle, optimizing internal biochemical milieu, and adjusting treatment times. The potential value of improving overall circadian functioning is shown in the work of Mormont et al in which pronounced rest-activity rhythms were associated with better survival in colorectal cancer patients receiving chronomodulated chemotherapy.

Lifestyle interventions that may improve circadian functioning involve diet, physical activity, and mind-body therapies. A diet that is anti-inflammatory and has appropriate carbohydrate intake, as well as regular meal timing, encourages normal circadian cycles. Adequate daytime physical activity encourages restful sleep, and morning light exposure during exercise may entrain melatonin rhythms. Meditation and other mind-body therapies can reduce anxiety and depression that may disrupt sleep. Aspects of the biochemical milieu that specifically disrupt circadian functioning are inflammation and stress hormones. Inflammation and cytokine disruption can be addressed with diet, herbs, and other natural substances.

Chronomodulation of chemotherapy in a US clinical setting will be discussed. A series of 12 cases will be presented of patients who experienced grade 3 to 4 toxicities with various chemotherapy regimens for colorectal cancer. When rechallenged with the same regimens administered chronotherapeutically, none of the patients experienced grade 3 to 4 toxicity.

**CONCLUSIONS:** Integrating lifestyle improvements, optimizing internal biochemical milieu, and adjusting treatment times has the potential to improve both the quality of life and disease outcomes in cancer patients.

## PSYCHOSOCIAL INTERVENTIONS

Lengacher, CA, V. Johnson-Mallard, J. Post-White, et al.

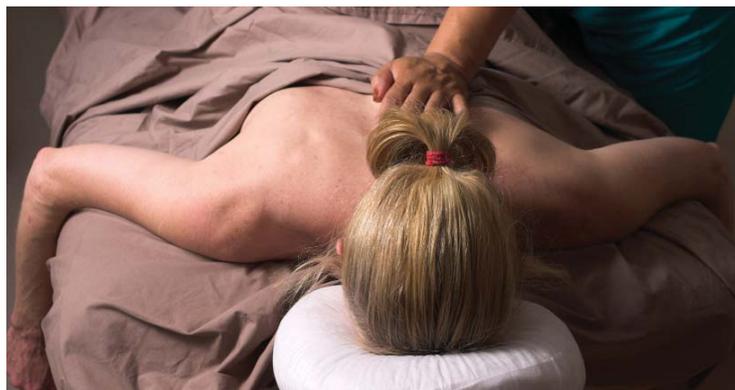
### Randomized Controlled Trial of Mindfulness-Based Stress Reduction (MBSR) for Survivors of Breast Cancer.

*Psychooncology*. 2009 December; 18(12): 1261-1272.

**OBJECTIVES:** Considerable morbidity persists among survivors of breast cancer (BC) including high levels of psychological stress, anxiety, depression, fear of recurrence, and physical symptoms including pain, fatigue, and sleep disturbances, and impaired quality of life. Effective interventions are needed during this difficult transitional period. **METHODS:** We conducted a randomized controlled trial of 84 female BC survivors (Stages 0-III) recruited from the H. Lee Moffitt Cancer and Research Institute. All subjects were within 18 months of treatment completion with surgery and adjuvant radiation and/or chemotherapy. Subjects were randomly assigned to a 6-week Mindfulness-Based Stress Reduction (MBSR) program designed to self-regulate arousal to stressful circumstances or symptoms (n541) or to usual care (n543). Outcome measures compared at 6 weeks by random assignment included validated measures of psychological status (depression, anxiety, perceived stress, fear of recurrence, optimism, social support) and psychological and physical subscales of quality of life (SF-36).

**RESULTS:** Compared with usual care, subjects assigned to MBSR(BC) had significantly lower (two-sided  $p < 0.05$ ) adjusted mean levels of depression (6.3 vs 9.6), anxiety (28.3 vs 33.0), and fear of recurrence (9.3 vs 11.6) at 6 weeks, along with higher energy (53.5 vs 49.2), physical functioning (50.1 vs 47.0), and physical role functioning (49.1 vs 42.8). In stratified analyses, subjects more compliant with MBSR tended to experience greater improvements in measures of energy and physical functioning.

**CONCLUSIONS:** Among BC survivors within 18 months of treatment completion, a 6-week MBSR(BC) program resulted in significant improvements in psychological status and quality of life compared with usual care.



## STUDY OF THE MONTH

Pace, A, D. Giannarelli, E. Galie, et al.

### Vitamin E Neuroprotection for Cisplatin Neuropathy: A Randomized, Placebo-Controlled Trial.

*Neurology*. 2010 March; 749: 762-766.

**OBJECTIVE:** The clinical use of cisplatin chemotherapy is limited by severe peripheral neurotoxicity reported in up to 90% of patients receiving a cumulative dose higher than 300 mg/m. The present study evaluates the neuroprotective effect of antioxidant supplementation (vitamin E) in patients treated with cisplatin chemotherapy. **METHODS:** A total of 108 patients treated with cisplatin chemotherapy were randomly assigned to receive vitamin E supplementation (alpha-tocopherol 400 mg/day) or placebo. Treatment was started orally before chemotherapy and continued for 3 months after the suspension of cisplatin.

**RESULTS:** Of 108 randomized patients, 68 received at least one clinical and neurophysiologic examination after cisplatin CT; 41 patients received a cumulative dose of cisplatin higher than 300 mg/m and were eligible for statistical analysis: 17 in the vitamin E group (group 1) and 24 in the placebo group (group 2). The incidence of neurotoxicity was significantly lower in group 1 (5.9%) than in group 2 (41.7%) ( $p < 0.01$ ). The severity of neurotoxicity, measured with a validated neurotoxicity score (Total Neuropathy Score [TNS]), was significantly lower in patients receiving vitamin E than those receiving placebo (mean TNS 1.4 vs 4.1;  $p < 0.01$ ).

**CONCLUSIONS:** This phase III study confirms the neuroprotective role of vitamin E against cisplatin peripheral neurotoxicity. Vitamin E supplementation should be adopted in patients receiving cisplatin-based chemotherapy. **CLASSIFICATION OF EVIDENCE:** This study provides Class II evidence that vitamin E supplementation significantly reduces the relative risk of developing signs or symptoms of neurotoxicity (relative risk = 0.14) (95% confidence interval = 0.02-1.00,  $p < 0.05$ ).

## NUTRITION

Campbell, MK, Carol Carr, Brenda DeVellis, et al.

### A Randomized Trial of Tailoring and Motivational Interviewing to Promote Fruit and Vegetable Consumption for Cancer Prevention and Control.

*Annals of Behavioral Medicine*. 2009 10; 382: 71-85..

**BACKGROUND:** Healthful dietary patterns, including eating fruits and vegetables (F&V) and avoiding obesity, may decrease the risk of cancer and other chronic diseases. In addition to promoting health for the general population, a cancer diagnosis may provide a "teachable moment," facilitating the adoption of more healthful eating habits and leading to lower risk of chronic disease and better overall health.

**PURPOSE:** This study was designed to test the effectiveness of two health communication interventions in increasing F&V consumption and physical activity in a sample of older adults (average age of 66 years), including both colorectal cancer (CRC) survivors and noncolorectal cancer-affected (N-CRC) individuals.

**METHODS:** CRC survivors and N-CRC individuals were recruited from a population-based case-control study and randomly assigned to four conditions using a 2 x 2 design. We tested two different methods of communicating and promoting health behavior change alone or in combination: tailored print communication (TPC) and brief telephone-based motivational interviewing (TMI).

**RESULTS:** A significant increase in F&V consumption was found for the combined intervention group in the entire sample ( $p < 0.05$ ). When stratified by cancer survivor status, the effect was concentrated in the N-CRC subset ( $p < 0.01$ ) versus CRC survivors. The combined intervention was also found to be most cost-effective for the N-CRC group, with TPC more cost-effective than TMI. For physical activity, none of the interventions produced statistically significant improvements.

**CONCLUSIONS:** This study indicates that combining tailoring and motivational interviewing may be an effective and cost-effective method for promoting dietary behavior change among older healthy adults. More research is needed to identify the optimal dose and timing for intervention strategies to promote dietary and physical activity change among both CRC survivors and the general population.

## ACUPUNCTURE



Crew, KD, J. L. Capodice, H. Greenlee, et al.

### Randomized, Blinded, Sham-Controlled Trial of Acupuncture for the Management of Aromatase Inhibitor-Associated Joint Symptoms in Women with Early-Stage Breast Cancer.

*Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* 2010 1 Mar; 287: 1154-1160. .

**PURPOSE:** Women with breast cancer (BC) treated with aromatase inhibitors (AIs) may experience joint symptoms that can lead to discontinuation of effective therapy. We examined whether acupuncture improves AI-induced arthralgias in women with early-stage BC. **METHODS:** We conducted a randomized, controlled, blinded study comparing true acupuncture (TA) versus sham acupuncture (SA) twice weekly for 6 weeks in postmenopausal women with BC who had self-reported musculoskeletal pain related to AIs. TA included full body/auricular acupuncture and joint-specific point prescriptions, whereas SA involved superficial needle insertion at nonacupoint locations. Outcome measures included the Brief Pain Inventory-Short Form (BPI-SF), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and Modified Score for the Assessment of Chronic Rheumatoid Affections of the Hands (M-SACRAH) obtained at baseline and at 3 and 6 weeks.

**RESULTS:** Of 51 women enrolled, 43 women were randomly assigned and 38 were evaluable. Baseline characteristics were comparable between the two groups. Our primary end point was the difference in mean BPI-SF worst pain scores at 6 weeks, which was lower for TA compared with SA (3.0 v 5.5;  $P < .001$ ). We also found differences between TA and SA in pain severity (2.6 v 4.5;  $P = .003$ ) and pain-related interference (2.5 v 4.5;  $P = .002$ ) at 6 weeks. Similar findings were seen for the WOMAC and M-SACRAH scores. The acupuncture intervention was well-tolerated.

**CONCLUSIONS:** Women with AI-induced arthralgias treated with TA had significant improvement of joint pain and stiffness, which was not seen with SA. Acupuncture is an effective and well-tolerated strategy for managing this common treatment-related side effect.

## PROSTATE CANCER

Cabrespine-Faugeras, A, M. Bayet-Robert, J. O. Bay, et al.

### Possible Benefits of Curcumin Regimen in Combination with Taxane Chemotherapy for Hormone-Refractory Prostate Cancer Treatment.

*Nutrition & Cancer.* 2010 622: 148-153.

Complementary and alternative therapies for neoplastic diseases treatment and prevention receive increasing attention from the medical community. Prostate cancer (PC) is the most frequently diagnosed malignancy and the second major cause of male death in industrialized countries. The chemopreventive properties and clinical safety of curcumin, a polyphenolic derivative, have already been established. However, curcumin regimen value in addition to conventional hormone refractory (HR) PC treatment remains largely unknown. This review article summarizes mechanisms by which curcumin may decrease HRPC aggressive proliferation and potentiate activity of taxane therapy.

**CONCLUSIONS:** Our analysis suggests that curcumin alone has a therapeutic value in HRPC. In combination with a taxane agent, this compound may enhance cytotoxicity and retard PC cell resistance to taxane. As a consequence, a rationale is provided for considering the possible benefits of curcumin regimen in combination with taxane therapy in HRPC patients.

## PSYCHOSOCIAL

Faul, LA, H. S. Jim, C. Williams, et al.

### Relationship of Stress Management Skill to Psychological Distress and Quality of Life in Adults with Cancer.

*Psychooncology*. 2010 Jan; 191: 102-109.

**BACKGROUND:** Distress is common among cancer patients, especially those undergoing chemotherapy. Although skill in stress management is often the target of intervention efforts, its relationship to distress and quality of life in patients about to begin cancer treatment has not been examined. **OBJECTIVE:** To examine the relationship of pre-treatment skill in stress management to patient distress and quality of life. **METHODS:** One hundred and ten adults diagnosed with stage I-IV cancer and ECOG  $\leq 2$  provided data on perceived stress management skill, anxiety, depression, and health-related quality of life prior to their initial chemotherapy infusion.

**RESULTS:** As predicted, greater skill in stress management was associated with lower levels of anxiety and depression and better overall mental quality of life. These relationships were generally independent of demographic and clinical variables also found to be associated with distress and quality of life.

**CONCLUSIONS:** Findings confirm that skill in stress management is related to pre-chemotherapy distress and quality of life and suggest the importance of assessing this variable as part of efforts to link distressed patients to appropriate psychosocial services. Findings also raise the possibility that assessing extant stress management skills could be used to match patients to the type of intervention most likely to benefit them.

## COLORECTAL CANCER

Larsson, SC, N. Orsini and A. Wolk.

### Vitamin B6 and Risk of Colorectal Cancer: A Meta-Analysis of Prospective Studies.

*JAMA : the journal of the American Medical Association*. 2010 17 Mar; 30311: 1077-1083.

**CONTEXT:** Mounting evidence indicates that vitamin B(6), a coenzyme involved in nearly 100 enzymatic reactions, may reduce the risk of colorectal cancer. **OBJECTIVE:** To conduct a systematic review with meta-analysis of prospective studies assessing the association of vitamin B(6) intake or blood levels of pyridoxal 5'-phosphate (PLP; the active form of vitamin B(6)) with risk of colorectal cancer. **DATA SOURCES:** Relevant studies were identified by a search of MEDLINE and EMBASE databases to February 2010, with no restrictions. We also reviewed reference lists from retrieved articles. **STUDY SELECTION:** We included prospective studies that reported relative risk (RR) estimates with 95% confidence intervals (CIs) for the association between vitamin B(6) intake or blood PLP levels and the risk of colorectal, colon, or rectal cancer. **DATA EXTRACTION:** Two authors independently extracted data and assessed study quality. Study-specific RRs were pooled using a random-effects model. **DATA SYNTHESIS:** Nine studies on vitamin B(6) intake and 4 studies on blood PLP levels were included in the meta-analysis. The pooled RRs of colorectal cancer for the highest vs lowest category of vitamin B(6) intake and blood PLP levels were 0.90 (95% CI, 0.75-1.07) and 0.52 (95% CI, 0.38-0.71), respectively. There was heterogeneity among studies of vitamin B(6) intake ( $P = .01$ ) but not among studies of blood PLP levels ( $P = .95$ ). Omitting 1 study that contributed substantially to the heterogeneity among studies of vitamin B(6) intake yielded a pooled RR of 0.80 (95% CI, 0.69-0.92). The risk of colorectal cancer decreased by 49% for every 100-pmol/mL increase (approximately 2 SDs) in blood PLP levels (RR, 0.51; 95% CI, 0.38-0.69).

**CONCLUSION:** Vitamin B(6) intake and blood PLP levels were inversely associated with the risk of colorectal cancer in this meta-analysis.

## MISTLETOE

Friedel, WE, H. Matthes, P. R. Bock et al.

**Systematic Evaluation of the Clinical Effects of Supportive Mistletoe Treatment within Chemo- and/or Radiotherapy Protocols and Long-Term Mistletoe Application in Nonmetastatic Colorectal Carcinoma: Multicenter, Controlled, Observational Cohort Study.**

*Journal of the Society for Integrative Oncology*. 2009 Fall; 74: 137-145.

In Europe, patients with colorectal carcinoma (CRC) frequently receive mistletoe extracts to improve quality of life and survival. This study was designed to evaluate supportive treatment with mistletoe extract Iscador (ISC) in nonmetastatic CRC patients under routine clinical conditions and to create well-founded hypotheses for future prospective clinical studies. The design of a multicenter, controlled, retrospective, observational cohort study with parallel groups met the Good Epidemiological Practice rules. Anonymous unselected standardized data from eligible patients with surgically treated stage I-III CRC and adjuvant therapy (AT) or conventional aftercare were included. End points were adjuvant therapy-related adverse reactions (AT-ADRs), symptoms, and disease-free survival (DFS). The results were adjusted for confounder effects. Eight hundred four (429 ISC vs 375 control) CRC patients from 26 centers were observed for a median of 58 versus 51 months; the median ISC therapy lasted 52 months. ISC patients showed fewer AT-ADRs (19% vs 48%,  $p < .001$ ) and fewer persisting symptoms ( $p < .001$ ). The DFS hazard ratio of 0.60 ( $p = .013$ ) suggests a survival benefit in ISC patients versus controls.

**CONCLUSIONS:** ISC was well tolerated without life-threatening ADRs, drug interactions, or tumor enhancement. These results suggest a beneficial effect of supportive care ISC therapy within AT protocols and long-term ISC treatment in stage I-III CRC patients, particularly improvement in AT-ADRs and symptoms and possible extension of DFS.



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